B3 CONT

polyphosphazenes, polyphosphates, polycaprolactone, polyhydroxybutyrates, polyesters, polyamides, polysaccharides, and polyproteins.

B4

66. (Amended) The composition of claim 2, further comprising a therapeutic agent, wherein said therapeutic agent is a ligand attached to the biomaterial architecture through a biomolecular interaction.

Please add the following new claims.

B5

73. (Amended) The composition of claim 2, wherein said biodegradable polymer is a copolymer of a polymer selected from the group consisting of poly(hydroxy acids), polyanhydrides, polyorthoesters, polyphosphazenes, polyphosphates, polycaprolactone, polyhydroxybutyrates, polyesters, polyamides, polysaccharides, and polyproteins.

Add B4

74. (Amended) The composition of claim 2, wherein said biodegradable polymer a blend of any of the polymers selected from the group of polymers consisting of poly(hydroxy acids), polyanhydrides, polyorthoesters, polyphosphazenes, polyphosphates, polycaprolactone, polyhydroxybutyrates, polyesters, polyamides, polysaccharides, and polyproteins.--

Remarks

It is requested that the foregoing amendment be entered and that the rejections be reconsidered. Claims 1-17 and 64-72 were examined in this case. Claims 1-17 and 64-72 stand rejected. In this response, claims 1, 2, 6, 8-10, and 66 have been amended, claims 73 and 74 have been newly added, and claims 4, 5, 14-54, 64, and 69-72 have been cancelled. Applicant submits that these amendments and additions do not present any new matter. Applicant additionally respectfully submits that in view of the arguments presented below, the claims are now in condition for allowance.

I. Addition, Amendment, and Cancellation of Claims:

Applicant has amended claims 1, 2, 6, 8-10, and 66 to more particularly claim the present invention, and Applicant asserts that support for these amendments can be found throughout the specification. Additionally, claims 73-74 have been newly added, support for which can also be found throughout the specification, e.g., at page 6, lines 20-23. In addition, claims 4, 5, 14-17, and 64 have been canceled in an effort to expedite prosecution. However, Applicant is not canceling these claims to concede the correctness of the Examiner's stated rejection. Rather Applicant explicitly reserves the right to pursue the subject matter of these claims in a continuing application. Finally, claims 18-54 and 69-72 have been canceled as being drawn to a non elected invention. Applicant reserves the right to pursue these canceled claims in a future divisional application

III. Rejection under 35 U.S.C. § 112, second paragraph:

The Examiner has rejected claims 1-17 and 64-68 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. This rejection has several aspects, which are addressed individually below.

The Examiner asserts that claims 1, 2, and 66 are unclear as to the use of "biological recognition event." In an effort to expedite prosecution, the term "biological recognition event" has been deleted from claims 1, 2, and 66. In claim 1, the term "biological recognition event" has been deleted and replaced with the term "anchor-adapter-tag unit," wherein the adapter interacts with an anchor and a tag simultaneously, support for which can be found on page 2, lines 15-19. In claim 2, the term "biological recognition event" has been replaced with "biomolecular interaction." The meaning of the term :"biomolecular interaction" is clearly set forth in the specification, for example at page 2, lines 15-19, which state that "this *biomolecular interaction* is achieved by using an '*anchor-adapter-tag*' system, in which an adapter which can interact specifically and with high selectivity with an anchor molecule (present on the biodegradable surface) and a tag (bound to the ligand to be immobilized) simultaneously is used

in attaching the ligand to the surface in a manner which is stable *in vitro* or *in vivo*." In light of the amendment to the claims, withdrawal of this aspect of the rejection is respectfully requested.

The Examiner asserts that claims 2, 6, 7, and 64-68 are unclear for the recitation of "biomaterial architecture." Applicant points out that the phrase "biomaterial architecture" is defined in the specification. Specifically, at page 6, lines 14-16, the specification states that "[t]he biomaterial architecture can be fabricated from any biodegradable and bioresorbable material that is capable of having an anchor moiety incorporated therein." The specification proceeds to teach some examples of biomaterial architecture by stating that "[i]n particularly preferred embodiments, the biomaterial architecture is a polymer" (page 6, lines 19-20). The specification proceeds to teach suitable polymers, which include "polymers of poly(hydroxy acids), polyanhydrides, polyorthoesters, polyphosphazenes, polyphosphates, polycaprolactone, polyhydroxybutyrates, polyesters, polyamides, polysaccharides, polyproteins, and any copolymers or blends thereof" (page 6, lines 20-23, see also lines 25-29). In light of these teachings, withdrawal of this aspect of the rejection is requested.

The Examiner states that the recitation of "involves" in claim 2 is unclear. In an effort to expedite prosecution, the word "involves" has been deleted from claim 2 and replaced with the phrase "comprises." In light of this amendment, withdrawal of this aspect of the rejection is requested.

The Examiner states that the use of process terminology, but not product by process terminology, in composition claims 2, 4, 5, and 8 is unclear. Claims 4 and 5 have been cancelled, rendering the present rejection to these claims moot. Applicant submits that claims 2 and 8, as amended herein, eliminate any process terminology and contain only composition terminology. Withdrawal of this aspect of the rejection is requested.

The Examiner states that the recitation of "biologically relevant molecule" in claims 6 and 64 is unclear. In order to expedite prosecution, Applicant has eliminated this term from claims 6 and 64. The claims now clearly recite what is meant by an anchor, a tag, and an adapter, without use of the term "biologically relevant molecule." Specifically, claim 6 recites the composition of claim 2, wherein the anchor is capable of being incorporated into the polymer

from which the biomaterial architecture is formulated, the tag is capable of attachment to the ligand, and wherein the adapter is capable of binding to both the anchor and tag moieties to generate a biomolecular interaction. Claim 66 recites the composition of claim 2, further comprising a therapeutic agent, wherein said therapeutic agent is a ligand attached to the biomaterial architecture through a biomolecular interaction. In light of the present amendment, Applicant requests withdrawal of this aspect of the rejection.

The Examiner states that the term "biomolecular interaction" in claims 6 and 64 is unclear. As pointed out above, the term "bimolecular interaction" is defined in the specification, see, e.g., page 2, lines 15-19; page 3, lines 3-4; and page 6, lines 18-19. In light of these teachings, withdrawal of this aspect of the rejection is requested.

The Examiner states that recitation of "desired ligand" in claims 6 and 64 is unclear. Applicant has deleted the word "desired" from the term "desired ligand" and request withdrawal of this aspect of the rejection.

The Examiner states that the term "PLA-PEG" in claim 9 is unclear and requests that the names of the compounds be used instead of their acronyms. Accordingly, the acronym "PLA-PEG" has been replaced with its compound name "poly(lactic acid)-co-poly(ethylene glycol)." Withdrawal of this aspect of the rejection is requested.

The Examiner states that claim 10 recites a Markush group improperly. Accordingly, claim 10 has been amended so that the Markush group is now recited properly. Applicant apologizes for this oversight and respectfully requests withdrawal of this aspect of the rejection.

III. <u>Rejection under 35 U.S.C. § 102(a):</u>

Claims 1-22, 13-15, 17-21, 24-30, 32-40, and 43-54 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Patel *et al.* (11/98). Claims 4, 5, 14-54 have been canceled, rendering the rejection to these claims moot. The Examiner states in the rejection that the Declaration by Dr Cannizaro filed October 3 is not persuasive because the declaration does not disclose facts in connection with what is in the publication. Accordingly, Applicant submits herewith new executed *Katz* declarations by the inventors, Scott M. Cannizzaro, Kevin

Shakeshiff, and Robert Langer, which properly point out that any description of the invention in Patel et al. was their contribution alone and the other authors listed on the reference were merely working under their direction. In light of these facts, Patel *et al* (11/98) is not an anticipatory reference because the invention was not known or used *by others* in this country, or patented or described in a printed publication in this or a foreign country before the invention thereof by the applicant for a patent. Applicant respectfully requests that the Examiner consider the new Katz declarations and withdraw the rejection under 35 U.S.C. § 102(a).

III. Rejection under 35 U.S.C. § 102(b):

Claims 1-14, 16, and 64-68 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Hoffman et. al. (Artificial Organs 16:43 1992)). The Examiner asserts that Hoffman discloses materials for use in tissue engineering that meet all of the limitations of each of the claims (e.g., nucleic acids and antibodies (pages 44-45)). Applicant disagrees.

Anticipation under 35 U.S.C. 102 requires that the invention disclosed by the prior art reference must be identical to the claimed invention in each and every aspect. As stated in *Hybritech Inc. v. Monoclonal Antibodies, Inc,* 802 F.2d 1367,231 U.S.P.Q. 81 (Fed. Cir. 1986), "[I]t is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention."

Claim 1, as amended herein, is directed to a composition comprising a biodegradable polymer having a ligand attached thereto, wherein said ligand is attached to said biodegradable polymer using an anchor-adapter-tag unit, wherein the adapter interacts with an anchor and a tag simultaneously. Amended claim 2 is directed to a composition comprising a biomaterial architecture having a ligand attached thereto through a biomolecular interaction, wherein said biomaterial architecture comprises a polymer having an anchor moiety incorporated therein or attached thereto, and wherein said biomolecular interaction further comprises an anchor-adapter-tag unit, whereby the tag is attached to the ligand, and wherein said adapter is bound to both the anchor and the tag to effect the biomolecular interaction. In an attempt to expedite prosecution, claims 4, 5, 64, and 14-17 have been canceled. Applicant is not canceling these claims to

concede the correctness of the Examiner's stated rejection and reserve the right to pursue these claims in future divisional applications.

As set forth in the amended claims, the invention relates to a three-component "anchor-adapter-tag" system in which an adapter can interact specifically and with high selectivity with an anchor (e.g., an anchor present on a biodegradable surface) and a tag (e.g., a tag bound to the ligand to be immobilized) simultaneously. The inventive anchor-adapter-tag system is used to attach a ligand to a surface in a manner that is stable *in vitro* or *in vivo* (see page 2, lines 15-19). The specification teaches that "because the biomolecular interaction involves an interaction between the anchor, the adaptor, and the tag, through the adapter, one or ordinary skill in the art will realize that the particular adaptor used must be able to interact with both the anchor and the tag." Thus, any multivalent adapter molecule with the necessary binding affinity for each of the components may be used" (page 7, lines 2-6). In but one example, the specification describes an anchor-adapter-tag system, wherein the anchor and tag are biotin and the adapter is avidin or streptavidin (see page 7, lines 6-7).

Turning to Hoffman et al., this reference generally discloses polymeric biomaterials that can be used as components of artificial organs, drug delivery devices, detoxicants, affinity separations systems, biosensors, diagnostic assays, and enzyme or cell bioprocessors (see page 44, column 2, lines 4-7). The biomaterials have incorporated into them a biological function, examples of which are drug/receptor, hormone/receptor, antigen/antibody, enzyme/substrate, or RNA or DNA hybridization interactions (see page 44, column 1, line 1 to column 2, line 3). The concept of building such interactions into soluble polymer molecules is illustrated in Figure 1. The Hoffman reference further discloses that "specific biological action may be built into macromolecular systems by combining them with the recognition biomolecule" (page 44, column 2, line 21 to page 45, line1). Examples of "recognition biomolecules" provided by Hoffman et al. include drugs that have been conjugated to polymers, which are further conjugated with antibodies for targeted drug delivery systems, and peptides that have been conjugated to soluble polymers and solid supports (page 45, column 1, lines 1-4 and 20-23).. These systems are further illustrated in Figure 2.

If the systems of Hoffman et al. are to be related to the present invention, they may be described as systems having an anchor and a tag. As shown in Figure 2, Hoffman et al. teaches immobilizing onto a polymer a biological recognition group (anchor) that can interact with a cell adhesion peptide (tag) that is located on the surface of a cell. Nowhere does Hoffman et al. teach of a third 'adapter' component that may be used to link together an anchor and a tag for the purpose of adhering a ligand, such as a cell or a drug, to the surface of a biodegradable polymer. Since the claimed invention requires that an adapter be included with a tag and an anchor, the Hoffman et al. reference does not anticipate the claimed invention.

In light of the above arguments, Applicant submits that Hoffman et al. does not contain every element of the claimed invention, and thus is not anticipatory under 35 U.S.C. § 102(b). Applicant respectfully requests withdrawal of this rejection.

Claims15 and 17 stand rejected under 35 U.S.C. § 102(b) as being anticipated by either one of Diamandis et al. (line. Chem. 37:625 (1991)) or Pardridge et al. (WO 92/22332) Specifically, the Examiner states that the claims describe no more than the biotin-avidin systems disclosed in the references. Claims 15 and 17 have been canceled by the present amendment, rendering the rejection to these claims moot. Applicant respectfully requests withdrawal of this rejection.

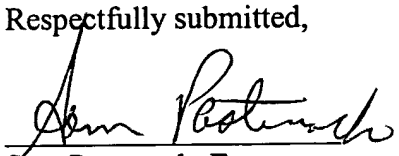
Conclusion

Based on the arguments presented above, it is submitted that the pending claims, as amended herein, are allowable over the art of record. Applicant would also like to thank the Examiner for thoughtful comments and careful consideration of the case. If a telephone conversation would help expedite prosecution of this case, please do not hesitate to contact the undersigned at (617) 248-5216.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."

Please charge any fees that may be required, or credit any overpayment, to our Deposit Account No. 03-1721.

Respectfully submitted,



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Dated: October 19, 2001

Version With Markings to Show Changes Made

In the Claims:

Claims 4, 5, 14-54, 64, and 69-72 have been canceled.

Claims 1, 2, 6, 8, 9, 10, and 66 have been amended as follows.

New claims 73-74 have been added.

1. (Amended) A composition comprising a biodegradable polymer having a ligand attached thereto, [and] wherein said ligand is attached to said biodegradable polymer using [a biological recognition event] an anchor-adapter-tag-unit, wherein the adapter interacts with an anchor and a tag simultaneously.

2. (Twice Amended) A composition comprising a biomaterial architecture having a ligand attached thereto through a [biological recognition event] biomolecular interaction, wherein said biomaterial architecture comprises a polymer having an anchor moiety incorporated therein or attached thereto, and wherein said [biological recognition event] biomolecular interaction [is further characterized in that it involves] further comprises an anchor-adapter-tag unit, whereby the tag is attached to the ligand, and wherein said adapter is [capable of binding] bound to both the anchor and the tag to effect the [biological recognition event] biomolecular interaction.

6. (Amended) The composition of claim 2, wherein the anchor [comprises a biologically relevant molecule] is capable of being incorporated into the polymer from which the biomaterial architecture is formulated, the tag [comprises a biologically relevant molecule] is capable of attachment to the [desired] ligand, and wherein the adapter [comprises a biologically relevant molecule] is capable of binding to both the anchor and tag moieties to generate a biomolecular interaction.

8. (Amended) The composition of claim 2, wherein said anchor is incorporated into the polymer [during polymer synthesis].

9. (Amended) The composition of claim 2, wherein said polymer is poly(lactic acid)-co-poly(ethylene glycol) (PLA-PEG).

10. (Amended) The composition of claim 2, wherein said biodegradable polymer is selected from the group consisting of polymers of poly(hydroxy acids), polyanhydrides, polyorthoesters, polyphosphazenes, polyphosphates, polycaprolactone, polyhydroxybutyrates, polyesters, polyamides, polysaccharides, and polyproteins[, copolymers or blends thereof].

66. (Amended) The composition of claim 2, further comprising a therapeutic agent, wherein said therapeutic agent is a ligand attached to the biomaterial architecture through a [biological recognition event] biomolecular interaction.

The following new claims have been added.

--73. (Amended) The composition of claim 2, wherein said biodegradable polymer is a copolymer of a polymer selected from the group consisting of poly(hydroxy acids), polyanhydrides, polyorthoesters, polyphosphazenes, polyphosphates, polycaprolactone, polyhydroxybutyrates, polyesters, polyamides, polysaccharides, and polyproteins.

74. (Amended) The composition of claim 2, wherein said biodegradable polymer a blend of any of the polymers selected from the group of polymers consisting of poly(hydroxy acids), polyanhydrides, polyorthoesters, polyphosphazenes, polyphosphates, polycaprolactone, polyhydroxybutyrates, polyesters, polyamides, polysaccharides, and polyproteins.--